## REMARKS

Reconsideration of this application is respectfully requested.

In response to the requirement for restriction, applicants have cancelled the non-elected claims. Applicants reserve the right to file a divisional application directed to the non-elected subject matter.

Claim 32 has been amended by incorporating the limitations of claim 35 into claim 32. Claim 35 has been cancelled. Amended claim 32 is also supported by paragraphs [0115], [0118], [0120], [0129], and original claims 8 and 22.

Claims 68-73 have been added to the application. These claims are supported by original claims 43 and 55, as well as paragraph [031] on page 8 of the specification.

Objection to the Specification

The Office indicated that this application contains sequence disclosures that are encompassed by the definition for nucleotide and/or amino acid sequences, but the application fails to comply with the requirements of 37 C.F.R. §1.821 through 1.825 because there is no sequence identifier for the nucleotide sequences in Figures 1A and 1B or in the "BRIEF DESCRIPTION OF THE DRAWINGS". Appropriate correction was required. Office Action at 2.

Figures 1A and 1B contain sequence identifiers for the amino acid and nucleotide sequences in the Figures. Specifically, these sequences are identified as SEQ ID NO: 1 and SEQ ID NO: 2, respectively, at the end of each sequence in the Figure. Paragraph [036] of the specification has been amended by inserting these sequence identifiers in the passage relating to the content of Figure 1. Accordingly, the objection to the specification may be withdrawn.

Finally, minor typographical and grammatical corrections have been made to paragraph [0116] of the application.

Double Patenting

Claims 40 and 41 were objected to under 37 C.F.R. §1.75 as being substantial duplicates of claims 34 and 35. Office Action at 3. This objection has been obviated by the cancellation of claims 34, 35, 40, and 41. Accordingly, applicants respectfully request that the objection be withdrawn.

Claim Rejections - 35 U.S.C. §112 - Definiteness

Claims 40, 41, and 43 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, which applicants regard as their invention. Office Action at 3. This ground for rejection has been obviated by the cancellation of claims 40, 41, and 43.

Claims 32-35, 37, 40, 41, and 43 were rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. According to the Office, the omitted steps are how to modulate the neuronal transport of the tetanus toxin or the fusion protein and whether the neuronal transport is modulated. According to the Office, the method step only refers the administration of the TrkB agonist, but fails to refer back to the preamble of the claimed method, i.e., modulating the transport in a neuron. Office Action at 3-4. Applicants respectfully traverse this ground for rejection and request reconsideration for the following reasons.

Claim 32 has been amended to recite that a Brain Derived Neurotrophic Factor or a Neurotrophin 4 is administered to a neuron "in an amount sufficient to thereby modulate the neuronal transport." Insertion of the word "thereby" links the administration of the Brain Derived Neurotrophic Factor or Neurotrophin 4 to modulation of neuronal transport in the neuron. Applicants courteously submit that the claims now properly refer back to the preamble of the claimed method. Accordingly, applicants submit that this ground for rejection may be withdrawn.

Claim Rejections - 35 U.S.C. §112 - Written Description

Claims 32-34, 40 and 43 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. According to the Office, the specification only discloses that BDNF and NT-4 can activate TrkB receptor (*see* specification, [014], [0118]). Further, according to the Office, the specification fails to disclose any other TrkB receptor agonist or any other neurotrophic factor that can activate TrkB receptor, and the specification fails to disclose the structural feature of TrkB receptor agonist that would activate TrkB receptor. Office Action at 4.

This ground for rejection has been obviated at least to the extent of the amendment of claim 32 to recite that the TrkB receptor agonist is "a Brain Derived Neurotrophic Factor (BDNF) or a Neurotrophin 4 (NT-4)." Since the Office has indicated that the specification contains adequate written description support for these embodiments of applicants' invention, applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn, at least to this extent.

Applicants submit that there is also adequate written description support for a "Glial-Derived Neurotrophic Factor (GDNF)," and have included this neurotrophic factor in the claims. Applicants investigated, *in vivo*, the influence of neurotrophic factors on neuronal localization and internalization of GFP-TTC and the mechanisms by which certain neurotrophic factors influence neuronal trafficking. They found that localization of GFP-TTC at the NMJ is rapidly induced by neurotrophic factors, such as Brain Derived Neurotrophic Factor (BDNF), Neurotrophin 4 (NT-4), and Glial-Derived Neurotrophic Factor (GDNF), but not by Nerve Growth Factor (NGF), Neurotrophin 3 (NT-3), and Ciliary Neurotrophic Factor (CNTF). Specification at ¶ [0115]. BDNF and NT-4 were found to increase the concentration of GFP-TTC at the NMJ, whereas NGF and NT-3 had no effect. Specification at ¶ [0118]. GDNF also induced GFP-TTC localization at the NMJ. Specification at ¶ [0120]. These teachings in applicants' specification provide ample written description support for the inclusion of GDNF in applicants' claims.

Claim Rejections - 35 U.S.C. §112 - Enablement

Claims 32-34, 40, and 43 were rejected under 35 U.S.C. §112, first paragraph. According to the Office, the specification is enabling for increasing the concentration of tetanus toxin or a fusion protein comprising a fragment C of the tetanus toxin in neuromuscular junction (NMJ) by injecting brain derived neurotrophic factor (BDNF) or neurotrophin (NT) 4 into Levator auris longus (LAL) muscle or gastrocnemius muscle of mice, but it does not reasonably provide enablement for a method of modulating the neuronal transport of the tetanus toxin or the fusion protein comprising a fragment C of

the tetanus toxin by using any TrkB receptor agonist other than BDNF and NT-4 *in vitro* or *in vivo*.

This ground for rejection has been obviated at least to the extent of the amendment of claim 32 to recite that the TrkB receptor agonist is "a Brain Derived Neurotrophic Factor or a Neurotrophin 4." Since the Office has indicated that the specification is enabling for the use of BDNF or NT-4, applicants respectfully request that this ground for rejection be reconsidered and withdrawn, at least to this extent.

Applicants' specification is also enabling for GDNF, which has been included in the claims. Applicants examined the effect of five trophic factors on GFP-TTC localization at the NMJ, including the neurotrophins NT-3, NT-4, and NGF, as well as the neurocytokine CNTF (Ciliary Neurotrophic Factor), a member of the LIF cytokine family, and GDNF (Glial-Derived Neurotrophic Factor), a member of the TGF-ß superfamily (Table 2). BDNF and NT-4 induced GFP-TTC localization at the NMJ. Applicants also reported that a level of induction similar to NT-4 was observed for GDNF (Table 2). Specification at ¶ [0129]. These results show that applicants' specification is also enabled for GDNF. Accordingly, reconsideration and withdrawal of the rejection based on enablement are respectfully requested.

In view of the foregoing amendments and remarks, favorable action at the Examiner's convenience is courteously solicited.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: October 2, 2006

By: _____

Kenneth J. Meyers
Reg. No. 25,146
Phone: 202-408-4033
Fax: 202-408-4400
Email: Ken.Meyers@finnegan.com

**Attachments:** Petition for Extension of Time and a check for $120.00